Weight-supported treadmill vs over-ground training for walking after acute incomplete SCI

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Abstract—Objective: To compare the efficacy of step training with body weight support on a treadmill (BWSTT) with over-ground practice to the efficacy of a defined over-ground mobility therapy (CONT) in patients with incomplete spinal cord injury (SCI) admitted for inpatient rehabilitation. **Methods:** A total of 146 subjects from six regional centers within 8 weeks of SCI were entered in a single-blinded, multicenter, randomized clinical trial (MRCT). Subjects were graded on the American Spinal Injury Association Impairment Scale (ASIA) as B, C, or D with levels from C5 to L3 and had a Functional Independence Measure for locomotion (FIM-L) score <4. They received 12 weeks of equal time of BWSTT or CONT. Primary outcomes were FIM-L for ASIA B and C subjects and walking speed for ASIA C and D subjects 6 months after SCI. **Results:** No significant differences were found at entry between treatment groups or at 6 months for FIM-L ($n = 108$) or walking speed and distance ($n = 72$). In the upper motor neuron (UMN) subjects, 35% of ASIA B, 92% of ASIA C, and all ASIA D subjects walked independently. Velocities for UMN ASIA C and D subjects were not significantly different for BWSTT (1.1 ± 0.6 m/s, $n = 30$) and CONT (1.1 ± 0.7 , $n = 25$) groups. **Conclusions:** The physical therapy strategies of body weight support on a treadmill and defined overground mobility therapy did not produce different outcomes. This finding was partly due to the unexpectedly high percentage of American Spinal Injury Association C subjects who achieved functional walking speeds, irrespective of treatment. The results provide new insight into disability after incomplete spinal cord injury and affirm the importance of the multicenter, randomized clinical trial to test rehabilitation strategies.

NEUROLOGY 2006;66:484–493

Annually, approximately 10,000 Americans have a traumatic spinal cord injury (SCI). For many patients, the most visible lingering disability is the inability to walk or a slow spastic-paretic gait with high energy cost.¹ A gait training strategy, using body weight support on a treadmill (BWSTT),^{2,3} has evolved from physiologic studies of the effects of the level and timing of limb loading during stepping and of stance and swing phase kinematics in spinal transected quadrupeds^{4–7} and in patients with complete SCI.^{8–10} The experimental intervention received clinical support from nonrandomized studies of patients with incomplete SCI early and late after injury.^{2,3,11–13} No randomized trials with blinded outcomes, however, had compared different physical therapy strategies aimed at the recovery of walking during initial inpatient and outpatient rehabilitation. Further, no prospective trials in SCI had col-

lected measures related to functional walking, such as walking speed, distance, and the need for assistive devices.^{14,15}

The Spinal Cord Injury Locomotor Trial (SCILT) was a single-blinded, parallel-group, multicenter, randomized clinical trial (MRCT) that compared two interventions for walking: BWSTT vs a similar intensity of a defined control (CONT) program of over-ground mobility training. Subjects had an incomplete SCI on admission to each site graded on the American Spinal Injury Association Impairment Scale (ASIA) as B, C, or D. The Functional Independence Measure locomotor (FIM-L) walking scores,¹⁶ obtained at inpatient admission and discharge from the participating clinical units (CUs) for the years 1997 and 1998, were used to formulate the study design.¹⁷ These data showed that 15% of patients classified as ASIA B, 40% as ASIA C, and 75% as

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*See the Appendix on page 492 for a list of Group members and Clinical Unit sites.

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Funded by the NIH at the National Institute for Child Health and Human Development grants RO1 H37439, R24 HD39629, and K01 HD013848; La Fondation Québécoise Sur La Moelle Epinière, and La Fondation Pour La Recherche Sur La Moelle Epinière.

Disclosure: The authors report no conflicts of interest.

Received November July 5, 2004. Accepted in final form December 12, 2005.

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ASIA D at the time of admission to the CU were able to walk 150 feet at a supervised or better level of function at discharge. Because of the divergence between the ASIA B and C subjects compared to the ASIA D subjects, the level of walking independence and the walking velocity were chosen as separate primary endpoints. The primary hypotheses were 1) ASIA B and C subjects in the BWSTT group will recover supervised or independent walking on the FIM-L with a reciprocal gait pattern for 150 feet ($FIM-L \geq 5$) significantly more often compared to those in the CONT group at 6 months after SCI and 2) ASIA D subjects assigned to BWSTT will walk over ground significantly faster than the CONT group.

Methods. *Study design.* The SCILT MRCT recruited potential subjects by screening all admissions to six CUs, each a regional SCI center, from June 2000 to January 2003. Coordination and central data management were carried out at the University of California Los Angeles. Institutional review board approval was obtained from each site. Written informed consent was obtained from each subject prior to inclusion. The design and methods for this trial, including efforts for training and standardizing therapies and data collection, have been reported in detail.¹⁷ A summary of important features follows.

Subject selection and randomization. Patients were entered within 8 weeks of onset of incomplete SCI and within 1 week of admission for rehabilitation. Subjects with a cervical to T10/T11 lesion were designated as the upper motor neuron (UMN) group. Subjects with a T11 to L3 lesion were designated as the lower motor neuron (LMN) group if they had no UMN neurologic signs. If subjects with a low thoracic lesion had UMN signs on one side and LMN signs on the other, they were designated UMN. Inclusion and exclusion criteria are listed in table 1. Subjects were excluded at time of randomization if they needed antispasticity medication other than overnight. After entry, use of medication was determined by the treating physician. Subjects were assigned to their treatment group using a random, permuted block design with the factors UMN-LMN and ASIA B-C-D across all CU sites and generated by the UCLA Statistical Coordinating Unit.

Treatment. All subjects received the CU's standard inpatient and outpatient rehabilitation therapies for mobility and self-care skills. Within this routine, the main component of their mobility training was 12 weeks of either BWSTT or CONT therapy for walking. They did not receive any formal training for walking other than during these sessions. The BWSTT group had its mobility training for up to 1 hour each day of therapy. The specific amount of time spent standing or stepping depended on each subject's level of exercise-induced fatigue. The physical therapists proceeded with stretching exercises for up to 10 minutes, then step training on the treadmill using BWS for 20 to 30 minutes in 3- to 10-minute increments. Walking over ground was practiced, once feasible, for an additional 10 to 20 minutes each session. For BWSTT, subjects wore a climbing harness (Robertson Harness, Henderson, NV) attached to an overhead lift that used a gas cylinder to enable vertical displacement during the step cycle (Vigor Co., Stevensville, MI). Weight support and treadmill speed were adjusted to enable training at speeds greater than 0.72 m/s with a goal of over 1.07 m/s.¹⁸ Stepping with partial weight support as needed was expected to allow therapists to initiate therapy for walking before patients were able to fully bear weight, prior to developing adequate motor control for balance and stepping, as well as allow practice of reciprocal stepping at faster speeds with greater safety and less fear of falling than early over-ground rehabilitation training would ordinarily permit. The trainers in the BWSTT group concentrated, both on and off the treadmill, on assisting trunk and lower extremity kinematics, limb loading, and the cutaneous and proprioceptive feedback that would approach those used by healthy subjects during reciprocal stepping. The SCILT trainer's group intermittently monitored the technique of BWSTT at each CU by videotape and provided help in solving training problems.

Table 1 Number of screened subjects excluded based on inclusion and exclusion criteria

By inclusion criteria

1. Ages 16–70 years (n = 98)
2. Traumatic SCI within 56 days of injury (n = 205)
3. Incomplete lesion (ASIA B, C, or D at time of randomization) from below C4 on at least one side of the body to no lower than L3 on either side of the body (n = 695)
4. Unable to ambulate over ground at randomization without at least moderate assistance (≤ 3 FIM locomotor score) (n = 125)
5. Mini-Mental State Examination score ≥ 26 (n = 32)

By exclusion criteria

1. Symptomatic orthostatic hypotension or >30 -mm Hg drop when upright in the BWS apparatus (n = 13)
2. Subject with a spine-stabilizing device whose treating surgeon states that BWSTT is contraindicated (n = 32)
3. Contraindication to weight bearing on lower extremities (pelvic or leg fracture, chronic joint pain) (n = 75)
4. Pressure sore stage 2 or higher, located where a harness or treadmill training or standing could affect healing (n = 52)
5. A debilitating disease prior to SCI that caused exercise intolerance and limited mobility-related self-care and instrumental activities of daily living (n = 157)
6. Must use antispasticity medication at entry (initial use to prevent spasms that interfere with sleep allowed) (n = 12)
7. Premorbid major depression or psychosis; suicide attempt caused the SCI (n = 55)
8. Unlikely to complete the intervention or return for follow-up (n = 102)
9. Participation in another research study (n = 1)

SCI = spinal cord; ASIA = American Spinal Injury Association Impairment Scale; FIM = Functional Independence Measure; BWS = body weight support; BWSTT = body weight support on a treadmill.

The CONT group also had its mobility training for up to 1 hour each day of therapy. The specific amount of time spent standing or stepping depended on each subject's level of exercise-induced fatigue. The physical therapists proceeded with stretching exercises for up to 10 minutes, followed by a minimum of 30 minutes of standing for those subjects who could not take steps. Subjects who could take steps practiced in parallel bars or over ground with assistive devices, braces, and physical assistance from one or two therapists within their exercise tolerance for 30 to 45 minutes. The CONT subjects were not allowed to use a treadmill or BWS.

The goals of BWSTT were not discussed with the therapists assigned to treat the CONT group. The two approaches were carried out at different locations within each CU. For both mobility interventions, practice aimed to progressively increase task difficulty, be repetitive, maintain the attention of subjects, and reinforce successful skill acquisition. Subjects were permitted to stand and walk, if feasible, during other portions of their inpatient and outpatient care, such as during routine occupational therapy and at home for daily activities. Both groups were permitted to perform leg and trunk strengthening exercises.

The maximum number of BWSTT or CONT sessions would have been 60 if subjects had received five sessions weekly for 12 weeks, or the equivalent of about 60 hours of formal mobility training. The number of training sessions was expected to vary among subjects from a minimum of 45 to the maximum of 60 sessions of their respective intervention. Treatment sessions could be stopped when individuals reached the highly func-

tional walking speed of 0.98 m/s, even if the minimum 45 sessions were not completed. After the assigned 12-week intervention (BWSTT or CONT), all subjects had the opportunity to receive conventional outpatient therapy if recommended by the treating physician. Adverse training events were monitored and reviewed by the external Safety and Data Monitoring Committee.

Outcome measures. The primary outcome measures included the FIM-L and over-ground walking speed. These tests were performed by trained, blinded observers at a site where they would not encounter subjects during treatment times. The internationally accepted standard for the FIM-L uses a 50-foot walk for levels 2 to 5 but requires a 150-foot walk for levels 6 and 7. A FIM-L score of 1 means the patient requires total physical assistance; 2, maximum assistance of 1 person; 3, moderate assistance; 4, minimal assistance (hands on contact); 5, supervision (not safe alone, but no physical help); 6, independent with equipment; and 7, no need for assistive devices.¹⁶ Walking speed was calculated for the faster of two 50-foot (15.2-meter) walks in patients who were able to walk that distance with moderate or less assistance. Patients were asked to walk as fast as safely possible. These outcomes were obtained at entry (baseline), every 2 weeks for 12 weeks, at the end of the training intervention (3 months), and at 6 and 12 months after entry into the study.

Secondary outcomes were collected at baseline and at 3, 6, and 12 months. They included the distance walked in 6 minutes to assess endurance and fitness,¹⁹ the Berg Balance Scale to assess trunk and leg motor control (range 0 to 56), the Walking Index for Spinal Cord Injury (WISCI) (range 0 to 20) to assess functional limitations that require braces and assistive devices,²⁰ the lower extremity motor score (LEMS) (range 0 to 50) to assess strength,²¹ the Ashworth scale for hypertonicity, and the SF-54 for self-perceived quality of life.²² Changes and interrelationships among these measures will be reported in other publications. Of the 7,406 forms with subject data expected from the coordinators and blinded observers at the CUs, 97% were complete when received by the Statistical Coordinating Unit.

Sample size. The FIM-L on admission and discharge from the participating CUs in 1997 to 1998 was used for a power analysis. We hypothesized a higher probability that ASIA B and C subjects receiving BWSTT would obtain a FIM-L score >4 than those receiving CONT. For a power of 0.92 with $\alpha = 0.05$ and a two-sided test, a total sample size of 50 ASIA B and 80 ASIA C subjects with UMN and LMN lesions was needed to demonstrate a difference in FIM-L scores. For a power of 0.84, a sample size of 80 ASIA D subjects who achieved over-ground walking at 6 months was expected to be needed to detect a >20% difference in walking speed.

Statistical analysis. A four-way design was employed with three stratification factors (UMN, LMN, CU site), one treatment factor, a repeated-measure time factor (onset of SCI to randomization), and the primary endpoint (FIM-L or walking speed) for ASIA B, C, and D entries. The analyses at baseline were conducted on those patients who had performance data such as walking speed available. For the intention-to-treat paradigm, the CUs asked subjects at the time they voluntarily withdrew from the trial to return for 3- and 6-month visits, but the institutional review boards would not permit an investigator to contact a subject who had withdrawn. The method of imputation was the last observation carried forward and included subjects who completed at least 6 weeks of mobility intervention.

Permutation tests and modified Fisher tests were used for the analyses of baseline data between the BWSTT and CONT groups. The 6-month analyses used a robust regression approach with a two-way design. Where the distributions were bimodal, a logistic regression analysis was performed using the standard asymptotic (Wald) or quasi-exact method. Ordinal or quantitative scales were split at a predetermined value (FIM-L score ≤ 4 or ≥ 5 , for example) and after examining histograms of the data distribution to derive a binary endpoint to carry out standard binary scale analyses. When data included outliers and influential points, we applied the Huber regression analysis to lessen the effects, for example, of the few very fast and very slow velocities in "outlier" subjects.²³

Results. Recruitment and retention. Figure 1 shows the flow diagram for recruitment. Of 1,434 screened pa-

Figure 1. Flow diagram of progress through the phases of screening, enrollment, allocation, follow-up, and data analyses of the SCILT. UMN = upper motor neuron group; LMN = lower motor neuron group; B, C, and D = ASIA classifications; BWSTT = step training using body weight support on a treadmill group; CONT = defined over-ground mobility control group.

tients with SCI admitted to the CUs, 422 potentially eligible subjects signed a consent form to allow further assessment, 156 were subsequently found to be eligible, 10 eligible subjects refused; 146 subjects were randomized into the MRCT. Table 1 shows the number of subjects excluded by each inclusion and exclusion criterion. Some individuals met more than one criterion that eliminated them from eligibility. The majority of excluded subjects had a complete SCI, onset beyond 8 weeks prior to admission for rehabilitation, or a FIM-L score >3. At a mean of 4.5 weeks after onset of SCI, 111 UMN and 35 LMN subjects were randomized. Eight UMN subjects (BWSTT, n = 6; CONT, n = 2) and five LMN subjects (BWSTT, n = 4; CONT, n = 1) dropped out prior to completing 6 weeks of intervention, mostly within the first week. Two of the subjects in the BWSTT group stopped because they felt the therapy was too taxing and two had a tendon or joint injury. Sixteen subjects, 10 UMN (BWSTT, n = 4; CONT, n = 6) and six LMN (BWSTT, n = 4; CONT, n = 2), did not meet the eligibility requirements because they had a FIM-L score of 4 at the time of randomization. They were inadvertently entered into the study and completed their respective mobility interventions. We carried out all analyses with these 16 subjects included (n = 133) and excluded (n = 117) and found no difference in the statistical outcomes. Data are reported only for the latter group.

Table 2 Baseline measurements for UMN and LMN subjects in intention-to-treat analyses

	B + C			C + D		
	BWSTT	CONT	<i>p</i>	BWSTT	CONT	<i>p</i>
No.	52	57		35	33	
Age, y	26 (16–68)	24 (16–61)	0.32	36 (17–69)	23 (17–61)	0.06
Gender			0.24			0.26
% Male	85	74		83	70	
% Female	15	26		17	30	
Race						
% White	48	68	0.08	51	58	0.30
% African American	34	19	40	21		
% Hispanic	10	11	6	15		
% Asian	6	0	3	0		
% Other	2	2	0	3		
Level						
% Cervical	67	54	0.33	66	55	0.54
% Thoracic	19	23	14	24		
% Lumbar	14	23	20	21		
Randomization, d	30 (7–56)	29 (10–56)	0.63	28 (7–56)	26 (10–56)	0.45
FIM-L score (0–7)	1.0 (1–1)	1.0 (1–1)	0.47	1.0 (1–2)	1.0 (1–2)	0.58
LEMS (0–50)	8.0 (0–19)	12.0 (2–20)	0.17	20.0 (13–25)	18.0 (13–26)	0.99
Speed, m/s	0	0	—	0	(n = 2; 0.2, 0.4)*	
Distance, m	0	0	—	0	0	—
Berg Balance Scale score (0–56)	3.0 (0–4)	3.0 (0–5)	0.11	4.0 (3–4)	4.0 (2–7)	0.38
WISCI (0–20)	0 (0–0)	0 (0–0)	0.20	0 (0–1)	0 (0–1)	0.16

Values are median (range). Group B + C includes all subjects used for intent-to-treat analyses of FIM-L score. Group C + D includes all subjects used for intent-to-treat analyses that were able to walk.

*Two subjects were able to walk in the CONT group.

UMN = upper motor neuron; LMN = lower motor neuron; BWSTT = step training using body weight support on a treadmill group; CONT = defined over-ground mobility control group; FIM-L = Functional Independence Measure locomotor; LEMS = lower extremity motor score; WISCI = Walking Index for Spinal Cord Injury.

For the intent-to-treat analyses of those who completed at least 6 weeks of intervention, 92 subjects were classified as UMN and 24 subjects were LMN. Fourteen of the UMN subjects (BWSTT, *n* = 6; CONT, *n* = 8) stopped before 12 weeks of mobility training was completed. Reasons for refusal to continue at any time after entry included disappointment at assignment, rapid recovery no longer requiring therapy, and rehabilitation therapy “too difficult.” No differences in rate or cause for withdrawal were observed between the BWSTT and CONT groups. The 6-month analyses for walking speed included 45 subjects with an UMN lesion initially graded ASIA C or D who completed their training and all outcome measures. The study fell short in recruiting ASIA D UMN and LMN subjects. Several CUs reported that ASIA D subjects no longer were being referred to their regional centers by 1999, instead going to community facilities.

Randomization. The baseline characteristics and outcome measures at the time of randomization are shown for subjects who had adequate data for the intention-to-treat analyses (*n* = 117) including UMN and LMN ASIA B and

C subjects (*n* = 109, table 2) and UMN and LMN ASIA C and D subjects who were able to complete the 50-foot walk (*n* = 69, table 2). The baseline characteristics of the BWSTT and CONT groups revealed no differences in age, gender, race, days since injury, or spinal level. FIM-L, LEMS, walking speed, walking distance, Berg Balance, and WISCI measures were also comparable at baseline, revealing that the subjects were highly disabled with only two of 117 patients able to walk 50 feet at entry, both who were in the CONT group.

Futility analysis and change in primary analysis. The FIM-L was originally planned for use in the primary outcome analysis of ASIA B and C subjects, whereas walking speed was planned for only ASIA D subjects, who were expected to become independent walkers regardless of assigned intervention. We did not enter a sufficient number of ASIA D subjects for this primary analysis. A comparison of BWSTT and CONT for walking speed in ASIA C and D subjects who were able to perform the task was originally planned as a secondary analysis, however. The majority of ASIA C subjects in the BWSTT and CONT groups reached functional walk-

ing scores, far more than predicted by the pre-study data gathered from the CUs. Thus, a change in the primary analyses was required. We combined the ASIA C and D subjects who could walk for the primary analysis of walking speed.

Prior to stopping the trial, a conditional power analysis was undertaken at the direction of the Safety and Data Monitoring Committee. Futility analyses based on available data revealed that to detect a conditional power of 80% for the primary outcome measure of FIM-L, an additional 2,500 subjects would have been needed. For a conditional power of 80% to detect a 20% difference in walking speed, an additional 4,000 ASIA C and D subjects would have been needed. Thus, we report the primary outcomes for those subjects enrolled by the time of the interim analyses for FIM-L in the ASIA B and C subjects and for walking speed for ASIA C and D subjects who were able to walk. We did not recruit a sufficient number of LMN subjects to complete independent analyses for those with conus/cauda equina SCI. We separately report the combined UMN and LMN subjects within each experimental group in the primary planned analysis as well as each UMN group as planned for a secondary analysis because mechanistic differences of the response to BWSTT may exist between individuals with UMN and LMN lesions.

Primary outcome analysis: ASIA B and C for FIM-L. The primary outcome measures were obtained at 6 months after entry, which was 3 months after BWSTT or CONT was completed. Statistical analyses were performed for intention to treat on data from ASIA B and C subjects who completed at least 6 weeks of intervention for UMN and LMN groups combined ($n = 109$) and for UMN subjects only ($n = 86$) (table 3). No statistical difference was found between the two groups for FIM-L score. Thirty-three percent (7/21) of ASIA B subjects in the BWSTT group were ambulatory at 6 months and 58% (14/24) in the CONT group. Of the ASIA B subjects who reached an FIM-L score >4 , 14 of 21 who achieved this score would have been randomized as ASIA C if entered at the maximum eligibility time of 8 weeks after SCI. The majority of ASIA C subjects recovered independent walking; 92% of BWSTT and CONT subjects (24/26 in each group) had a FIM-L score ≥ 6 at 6 months. ASIA C subjects were significantly more likely than ASIA B subjects to walk independently and both ASIA B and C subjects who were randomized earlier (<4 weeks after SCI) had a greater probability of recovery to a FIM-L score >5 (table 3).

Primary outcome analyses: ASIA C and D for walking speed. Intent-to-treat analyses were performed on data from 68 UMN and LMN subjects graded ASIA C and D who could walk over ground and completed at least 6 weeks of intervention as well as on 55 of the UMN subjects (table 4). No statistical differences between treatment groups were observed in walking velocity at 6 months for the combined UMN/LMN subjects or the UMN subjects alone. The median measures for velocity in the ASIA C and D subjects demonstrated a remarkably high level of walking ability and fell within the range of functional community ambulation.

Secondary outcome analyses: UMN ASIA C and D at 6 months. The median quartile walking velocities at 6

months for UMN ASIA C and D subjects were unexpectedly high in both arms (1.1 m/s [table 5]). These analyses were performed on the 26 of 27 BWSTT and 16 of 17 CONT subjects at 6 months who could complete the walking test. Regardless of the method of statistical analysis carried out on the ASIA C and D groups, including the effect by CU and time since onset of SCI, no significant differences were found between the two interventions for FIM-L, walking speed, endurance, LEMS, Berg Balance Scale score, or WISCI score.

Figure 2 shows the change in walking speed at 3 months compared to 6 months for ASIA B, C, and D subjects who were walking and illustrates the overlap in walking speeds for the two arms of the trial. This figure also illustrates the change from entry, when walking speed was zero for these subjects, to the velocities attained at 3 or 6 months. Walking speed at the end of treatment was highly correlated ($r = 0.91$) with the speed at 6 months, but speeds continued to increase between 3 and 6 months. Earlier time of entry (<4 weeks) into the MRCT after onset of SCI was associated with faster walking speeds ($p = 0.001$) and longer walking distances ($p = 0.0001$) in both arms at 6 months for each ASIA group compared to velocities attained in subjects in that group who were randomized >4 weeks after SCI. This finding was primarily related to subjects who were entered at a lower ASIA level at <4 weeks after SCI (e.g., ASIA B or C) and attained the next higher ASIA level (e.g., ASIA C or D) within the next 4 to 6 weeks.

The number of treatment sessions was higher ($p = 0.01$) in the BWSTT group (51.5 ± 9.3) than the CONT (40 ± 16) for the intention-to-treat analysis of all UMN and LMN subjects. This difference was found, however, only for the ASIA C subjects. The difference in the number of sessions was attributable in part to a higher number of individuals in the CONT group who reached the maximum walking speed of 0.98 m/s prior to completion of the minimum 45 sessions. Either the subjects or their therapists determined that they had no need to continue CONT rehabilitation for gait training. An analysis of only the UMN subjects, however, revealed no significant difference in number of treatment sessions for the combination of B, C, and D subjects or for the ASIA C subjects in each arm of the trial.

Adverse responses. No differences in adverse reactions were found between the two arms during treatment. Most complications during rehabilitation were not related to the interventions. No excess muscle strain, joint pain, or other potential complications of mobility training were documented from a list on one of the report forms. Based on questions 21 and 22 about pain from the SF-54, no differences were found. Based on the Ashworth score, no differences in tone of the lower extremities or frequency of spasms at 6 or 12 months were found for UMN subjects randomized to each intervention.

Discussion. No significant differences were observed at 6 months for the FIM-L for ASIA B and C subjects or in walking velocity for ASIA C and D subjects between the BWSTT and CONT groups. These individuals represented incomplete SCI patients referred to the regional rehabilitation centers

Table 3 FIM-L at 6 months for ASIA B and C subjects (analysis of maximum likelihood estimates)

	BWSTT		CONT		<i>p</i>
	No.	FIM	No.	FIM	
UMN and LMN B, C	52	6 (1–6)	57	6 (2–6)	0.39
ASIA B < C	21	24			<0.001
Shorter time of SCI to randomization					0.07
UMN B, C	42	6 (1–6)	44	5 (1–6)	0.98
ASIA B < C	16	18			<0.001
Shorter time of SCI to randomization					0.03

Values for FIM are given as medians (interquartile range).

FIM-L = Functional Independence Measure locomotor; ASIA = American Spinal Injury Association Impairment Scale; BWSTT = step training using body weight support on a treadmill group; CONT = defined over-ground mobility control group; UMN = upper motor neuron; LMN = lower motor neuron; SCI = spinal cord injury.

who fulfilled the inclusion/exclusion criteria and could not ambulate without human assistance. Subjects were similar in demographics and outcome measures at baseline, suggesting successful randomization. The “median” UMN subject who was initially graded ASIA C or D on admission to a SCILT CU became able to walk independently by 6 months after SCI at velocities that usually allow unlimited community activity.²⁴ For UMN C and D subjects, the outcomes were internally consistent at the primary endpoint of 6 months in terms of walking speed, distance, and level of independence, which occurred in parallel to gains in leg strength (LEMS) and Berg Balance Scale score (table 5). Thus, both internal and external validity of the results is likely.

For UMN ASIA B subjects, neither treatment led to gains in over-ground walking. Most of the subjects who did improve to have a measurable walking speed were entered as ASIA B soon after SCI and converted to ASIA C within the 8-week entry period (but continued to be considered as

ASIA B for data analysis). Thus, patients who are still graded ASIA B at 8 weeks after SCI have a low probability of achieving functional walking with a FIM-L score ≥ 4 when treated with either BWSTT or CONT.

The ASIA C and D subjects in both treatment groups achieved walking abilities beyond what had been expected (figure 2) based on the available literature at the start of SCILT and the experience of the investigators.^{25,26} Based on data collected in 1997 from the SCILT sites, no more than 60% of ASIA C patients were expected to walk at discharge from the inpatient service with a FIM-L score > 4 .¹⁷ At the interim analysis, 92% of ASIA C and D subjects in the CONT group were able to walk and 78% performed at walking velocities greater than 0.8 m/s. The ASIA C and D subjects in the BWSTT group also reached these levels of walking ability. The trial was stopped before the planned number of ASIA D subjects was recruited based on the outcome of the futility analyses; results were reported on those subjects entered by the time of completion of the interim analyses. We did not enter enough subjects with conus/cauda equina SCI, which represents about 20% of traumatic SCI, to be able to make an independent analysis of LMN subjects.

For patients graded as ASIA C on admission for rehabilitation, the SCILT revealed less disability related to walking by 6 months after SCI than had been assumed from studies performed at single sites. In SCILT, most individuals graded ASIA C (24/26 BWSTT; 24/26 CONT) at entry became able to walk independently. Attained velocities for UMN ASIA C and D individuals also did not differ between BWSTT and CONT groups (median 1.1 and 1.0 m/s; table 4). Walking speeds were so much faster than expected that the hypothesized 20% increase using BWSTT that was used for the statistical power analysis would not have been clinically meaningful even if present. No prior studies had reported the walking speeds achieved during rehabilitation. Indeed, few data were available in the literature about walking-related outcomes after SCI. The 24 sites that participated in

Table 4 Walking speed at 6 months for ASIA C and D subjects (analysis of maximum likelihood estimates)

	BWSTT		CONT		Estimate	SE	95% CI	<i>p</i>
	No.	m/s	No.	m/s				
UMN, LMN C, D	35	1.1 (0.8–1.4)	33	1.0 (0.7–1.5)	−0.06	0.13	−0.31 to 0.19	0.65
Shorter time of SCI to randomization					−0.02	0.01	−0.02 to 0.01	<0.001
UMN C, D	30	1.0 (0.6–1.5)	25	1.2 (0.9–1.7)	−0.08	0.16	−0.40 to 0.22	0.58
Shorter time of SCI to randomization					−0.02	0.004	−0.03 to 0.01	<0.001

Values for walking speed are given as medians (interquartile range).

ASIA = American Spinal Injury Association Impairment Scale; BWSTT = step training using body weight support on a treadmill group; CONT = defined over-ground mobility control group; UMN = upper motor neuron; LMN = lower motor neuron; SCI = spinal cord injury.

Table 5 Secondary outcome measures for UMN C and D subjects who were able to walk at 6 months

Measure	Baseline			6 Months		
	BWSTT	CONT	<i>p</i>	BWSTT	CONT	<i>p</i>
No.	27	18	27	18		
FIM-L (0–7)	1.0 (1–1)	1 (1–1)	0.44	6 (6–7)	6 (6–7)	0.69
Speed, m/s	—	—	1.1 (0.6–1.5)	1.1 (0.4–1.7)	0.98	
Distance, m	—	—	312 (165–477)	401 (366–483)	0.27	
LEMS (0–50)	22 (16–27)	25 (15–27)	0.85	45 (43–49)	45 (36–49)	0.45
Berg (0–56)	4 (3–4)	4 (0–4)	0.66	52 (35–56)	55 (40–56)	0.77
WISCI (0–20)	0 (0–1)	0 (0–1)	0.30	18 (13–19)	18 (13–19)	0.69

Values are given as median (interquartile range).

UMN = upper motor neuron; BWSTT = step training using body weight support on a treadmill group; CONT = defined over-ground mobility control group; FIM-L = Functional Independence Measure locomotor; LEMS = lower extremity motor score; WISCI = Walking Index for Spinal Cord Injury.

the Model SCI Care Systems (National Institute on Disability and Rehabilitation Research, www.spinalcord.uab.edu) did not routinely collect walking outcomes from 1973 to 2000 on their 15,000 subjects.¹⁴ One Model Systems site reported that only 10% of incomplete paraplegic and 13% of incomplete tetraplegic patients (711 subjects) regained the ability to walk 50 meters or climb stairs,²⁵ whereas another site reported that 66% (43/64) of incomplete ASIA C and D tetraplegic subjects could ambulate 50 feet independently at discharge.²⁶ The interaction between time of assignment of the ASIA score, the initial level of walking skill, and the functionality of ambulation in terms of speed and endurance, however, was not discernible from the reports. Also, no information was available before the start of SCILT about the use of standardized measures for walking speed and distance or need for assistive devices.

The Sygen MRCT, published after the start of

SCILT, compared GM-1 ganglioside to placebo.²⁷ Modified Benzel scores, which expand the ASIA grades, were assigned within 24 hours of a UMN SCI. Benzel grade V is defined as walking with or without physical assistance for 25 feet, which has no equivalent to a FIM-L measure. Of interest, this Benzel grade was achieved 26 weeks after entry by 2% (9/482) of Sygen study subjects initially graded ASIA A, 30% (39/131) for ASIA B, and 94% (94/100) for ASIA C. In the latter group, 59/100 became unlimited walkers by the Benzel system. Walking speed and endurance were not reported. SCILT subjects received their ASIA grade well beyond 24 hours after SCI, so one might have expected to have even fewer ASIA B and C subjects who still could not walk 2 to 8 weeks after SCI to subsequently achieve an FIM-L score >4. Thus, the natural history of disability after incomplete SCI may be considerably different from what had been assumed prior to the Sygen and SCILT MRCTs.

The results did not support the expectation that BWSTT would be more effective than CONT therapy. Studies published before and after the start of SCILT reported positive results for similar BWSTT approaches.^{3,12,13,28–30} However, most of these studies found improvements in individuals with chronic SCI. Also, no alternative treatment or concurrent control group was used. For example, Wernig et al.³ showed that 33 of 36 (91%) wheelchair-bound patients with a recent myelopathy, most of whom had a traumatic SCI, recovered the ability to walk at least five steps. In comparison, only 12 of 24 of the site's historical control subjects treated with conventional therapy accomplished this level of walking. The subjects were not randomized to a comparison intervention other than BWSTT and outcome measures were not blinded. Walking speed and distance were not reported. The LEMS score of subjects at the start of treatment (median of 7 to 8 weeks after spinal cord

Figure 2. Comparison of walking speed at end of intervention (3 months) and at time of primary outcome analysis in ASIA B, C, and D subjects who were able to walk and had complete data at 6 months.

disease symptoms) ranged from 15 to 38. Most patients with an LEMS score >20 will recover the ability to take steps for at least short distances.³¹ Of the UMN ASIA C and D subjects in SCILT who were unable to walk at entry, 94% (BWSTT 35/37 and CONT 31/33) walked at least 150 feet without assistance. Thus, the Wernig et al. study cannot be interpreted as showing that BWSTT is more efficacious than training without BWS on a treadmill.

Rehabilitation trials may fail to reveal a difference between an experimental and control therapy because they do not provide the necessary dose of the experimental treatment³² or do not maintain sufficient differences between the experimental and control interventions. We standardized the CONT mobility therapy to include similar intensities of weight bearing for standing or, when feasible, time spent training to walk. The number of mobility training sessions for the CONT and BWSTT group aimed to be equal. This was achieved for the ASIA B and D subjects and the UMN ASIA C subjects. Although a trend was present for the BWSTT groups to have received more therapy sessions than the CONT, the two arms had equal outcomes.

The ability of the CONT and BWSTT subjects to take steps over ground determined how much they would practice walking on level surfaces in each session. If patients developed the ability to take steps, usual rehabilitation care proceeded to try to improve over-ground walking skills. Possibly, the intensity of therapy for walking in both treatment groups may have been greater than what some rehabilitation providers offer to their physically assisted walkers who are graded ASIA C. The SCILT cannot directly address this possibility since other intensities of mobility-related activity were not studied. One of the rationales for BWSTT was to allow earlier step training and a higher intensity of initial practice. The contrast in the amount of standing and stepping between the two groups, however, was probably less than anticipated. Subjects in the CONT and BWSTT groups were required to weight bear or practice walking, when feasible, for similar amounts of time. The MRCT's primary aim was to compare the potential advantages of BWSTT to CONT within similar practice durations, not to compare different amounts of therapy time. The early gains by ASIA C and D subjects in both arms by 5 weeks after entry (data not shown) and by the end of 12 weeks of training compared to the more modest additional gains in walking speed by 6 months (figure 2), suggest that BWSTT may, in effect, have become only a marginally different training strategy than CONT during the intervention, at least in terms of intensity of early practice of walking. The trial, however, was designed to test two treatment strategies and found that they were equivalent for the outcomes measured. The better than expected

walking velocity outcomes in ASIA C subjects in SCILT may also be attributed in part to the emphasis on task-oriented therapy for all subjects, the entry of subjects without serious comorbidities, and a preponderance of patients with cervical central cord injuries who have a fair prognosis for recovery of walking.³³ Given that BWSTT and CONT provided equivalent outcomes for subjects in SCILT, clinicians and patients can base their use of each strategy on personal preferences, skill, availability of equipment, and costs.

BWSTT for ASIA B subjects with UMN lesions did not improve outcomes over CONT therapy. BWSTT was expected to induce mechanisms of activity-dependent plasticity within the spinal cord, which would be reflected in locomotor gains.³⁴ If mechanisms of spinal plasticity in humans are to be used for functional walking, greater supraspinal input or other interventions that modulate posture and spinal stepping oscillators will be necessary. The highly functional outcomes in most of the ASIA C and D subjects regardless of the intervention suggest that when some threshold of supraspinal input and segmental sensory feedback are available, task-specific training can lead to improved walking.

Interventions that meet criteria for success, such as training hind limb stepping in spinal transected cats and rats or employing a physical therapy strategy for walking in single-subject designs, are critical for the development of new rehabilitation therapies to improve motor control. The results of these types of experiments may support further scientific study of a new intervention, but the experiments cannot stand alone as evidence of the efficacy of the approach. The results of SCILT reemphasize the value of MRCTs with blinded outcomes in rehabilitation research, especially to evaluate new and complex physical therapies. Statistically sound MRCTs in neurorehabilitation with adequate numbers of subjects, distinctively defined interventions, blinded outcomes, and relevant outcome measures had only been attempted several times prior to SCILT.^{35,36} This study demonstrated that complicated physical therapy approaches can be taught to therapists and implemented across sites. The SCILT confirmed the feasibility of carrying out an ethical, scientifically rigorous trial within the time and physical constraints of customary inpatient and outpatient services. The results also provided quantitative data about functional outcomes after SCI that differ from reports of volunteer subjects from a single site, which will improve power analysis calculations for future trials that assess recovery of walking.

Future trials of BWSTT may aim to improve outcomes in ASIA B subjects who have no motor control beyond 8 weeks after SCI and in ASIA C subjects who still cannot walk more than 4 to 6 months after SCI. Pilot studies of chronic ASIA C

patients who cannot walk suggest that the combination of BWSTT with functional electrical stimulation or robotic assistive devices may improve stepping.^{37,38} BWSTT may be a valuable training adjunct in future trials of biologic interventions that promote axonal regeneration toward the lumbar cord to physiologically incorporate this input³⁹ because the technique may be less physically burdensome on therapists and safer for assisting ASIA A and B subjects to stand and step than conventional physical therapy. Testing these approaches will require well-designed MRCTs.

Acknowledgment

The authors thank the staff of each rehabilitation center and the individuals who participated in this study. They also thank Dr. Walter Hauck and Dr. Ralph Marino for their suggestions on this manuscript.

Appendix

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Corrections

Vascular events, mortality, and preventive therapy following ischemic stroke in the elderly

In the article "Vascular events, mortality, and preventive therapy following ischemic stroke in the elderly" by R.C. Kaplan, D.L. Tirschwell, W.T. Longstreth, Jr., et al., (*Neurology* 2005;65:835–842), a data coding error led to incorrect classification of recurrent strokes into the categories of ischemic, hemorrhagic, or indeterminate etiology. The following correction in the Results section (p. 837, first paragraph) is required: *Of recurrent strokes, 85.8% (n = 103) were ischemic, 7.5% (n = 9) were hemorrhagic, and 6.7% (n = 8) were of indeterminate etiology.* In addition, two statements in the first paragraph of the Discussion (p. 839) are incorrect. The proportion of hemorrhagic strokes among recurrent stroke events should have been stated as 7.5% rather than 20%. The authors also incorrectly stated that the study suggested a higher proportion of hemorrhagic strokes among recurrences than prior studies of stroke survivors. The authors regret the errors.

Plasma cells in muscle in inclusion body myositis and polymyositis

In the article "Plasma cells in muscle in inclusion body myositis and polymyositis" (*Neurology* 2005;65:1782–1787) by S.A. Greenberg, E.M. Bradshaw, J.L. Pinkus, G.S. Pinkus, T. Burleson, B. Due, L. Bregoli, K.C. O'Connor, and A.A. Amato, the author L. Bregoli was incorreccted listed as L.S. Bregoli. The authors regret the error.

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Vascular events, mortality, and preventive therapy following ischemic stroke in the elderly

Neurology 2006;66;493
DOI 10.1212/WNL.66.4.493

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